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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 09/773,374 | 02/01/2001 | Bing-Yan Zhu | 044481-5058 | 4008 |

9629 7590 04/05/2002

MORGAN LEWIS & BOCKIUS LLP
1111 PENNSYLVANIA AVENUE NW
WASHINGTON, DC 20004

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| EXAMINER |
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TRUONG, TAMTHOM NGO

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| ART UNIT | PAPER NUMBER |
|----------|--------------|

1624

DATE MAILED: 04/05/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/773,374

Applicant(s)

ZHU ET AL.

Examiner

Tamthom N. Truong

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-16 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on ____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). ____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The following reasons apply:

- a. There is double inclusion in the definitions of R^1 and/or R^{14} , for example, C_0 -alkyl-OH is the same as $-OR^2$ (with R^2 as hydrogen).
- b. Typographical errors in several places, for example, variables " r^6 " and " r^{18} " are believed to be " R^6 " and " R^{18} ". Correction is solicited for consistency.
- c. The term "prodrug derivatives" is vague because it does not refer to a definite chemical structure. Page 31 describes what a prodrug derivative is. However, such description still does not set the metes and bounds for a prodrug derivative because one cannot visualize the final structure of said derivative.

d. The term “containing” in the definition of “heterocyclic ring” is open-ended, and does not exclude atoms other than those recited. Applicant is suggested to replace the word “containing” with “having”.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. **Scope of Enablement:** Claims 1-16 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the preparation and use of compounds of substituted quinolinone or quinoxalinone, does not reasonably provide enablement for the preparation and use of their “prodrug derivatives”. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The following factors have been considered in the determination of an enabling disclosure:

- (1) The quantity of experimentation necessary;
- (2) The amount of direction or guidance presented;
- (3) The state of the prior art;
- (4) The relative skill of those in the art;
- (5) The predictability or unpredictability of the art;

(6) The breadth of the claims;

[See *Ex parte Forman*, 230 USPQ 546 (Bd. Pat. App. & Int., 1986); also *In re Wands*, 858 F. 2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988)].

The specification only describes “prodrug derivatives” in a generic sense, and refers to the text of Bundgard for further guidance. While it is true that a prodrug derivative typically has an additional ester or amide group on the compound. However, the location of such ester or amide group is also critical. Selecting the site of attachment for said group would require undue experimentation, let alone selecting what moieties to constitute such an ester or amide group. Furthermore, the active metabolites from a prodrug derivative may or may not have the same activity as the intended compound. Thus, the pharmacokinetic of a prodrug derivative requires an extensive research. Thus, given the unpredictable nature of the art, and the limited guidance provided, the skilled scientist would have to carry out undue experimentation to make a prodrug derivative of a compound claimed herein.

Claims 14 and 15 are also not enabled for a method of preventing “a condition....characterized by undesired thrombosis” and/or the many diseases recited herein. The specification does not provide guidelines as to the dosage for prevention, the onset and duration of prevention, etc. Thus, for the prevention of the many diseases claimed herein, one skilled in the art will have to carry out undue experimentation to select a course of prevention for said diseases.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1, 2, and 13-16 are rejected under 35 U.S.C. 102(a) as being anticipated by **Dudley et. al.** (WO 99/50254). For example, on page 24, line 9, Dudley et. al. discloses a compound by the name, *1-(3-Diethylamino-propyl)-3-phenyl-1H-quinoxalin-2-one*. Said compound is embraced by the formulae in claims 1 and 2, with the following substituents:

- i. A is R², and R² is hydrogen;
- ii. n and m are both 0; Z and D are direct links;
- iii. R¹ is hydrogen; R¹¹ represents C₆₋₁₂ carbocyclic aryl;
- iv. X is N; E and J are direct links;
- v. G is (CH₂)_t-(C=O)_u-NR¹⁸R¹⁹;
- vi. p = 3; t = 0, and u = 0; or
- vii. p = 2; t = 1, and u = 0
(i.e., G is either -NR¹⁸R¹⁹, or -CH₂-NR¹⁸R¹⁹);
- viii. R¹⁸ and R¹⁹ are C₁₋₈ alkyl.

The disclosed compound also has the ability to inhibit factor Xa, and act as an antithrombotic agent, or an anti-coagulant. Thus, it can treat many of the diseases as claimed

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herein as well as coating stents and devices, or sustaining biological sample in an anticoagulant state (see pages 41, and 70 of US'254). Therefore, at the time of the invention, one skilled in the art would have known how to make and use claimed compounds having structures similar to the one taught by Dudley et. al.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tamthom N. Truong whose telephone number is 703-305-4485. The examiner can normally be reached on M-F (9:00-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mukund Shah can be reached on 703-308-4716. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4556 for regular communications and 703-308-4556 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235.

Tamthom N. Truong
Examiner
Art Unit 1624



April 5, 2002